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In Vitro Comparison of Amifloxacin and Six Other Antibiotics Against Aminoglycoside-Resistant *Pseudomonas aeruginosa*

KENNETH D. THOMPSON,[1]* J. PAUL O'KEEFE,[2] AND WALTER A. TATAROWICZ[1,2]

Departments of Pathology[1] and Medicine,[2] Loyola University Medical School, Maywood, Illinois 60153

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The in vitro activity of the synthetic fluoroquinolone amifloxacin was compared with those of six other antibiotics: ampicillin, aztreonam, cefotaxime, cephalexin, cinoxacin, and gentamicin. Amifloxacin had the lowest 50% MIC of any of the antibiotics tested against aminoglycoside-resistant *Pseudomonas aeruginosa*, 4 μg/ml.

Nosocomial infections due to resistant organisms, such as *Pseudomonas aeruginosa*, have become common (5, 6, 9). These infections usually require the use of toxic or expensive antibiotics. Additionally, resistance to antibiotics, including aminoglycosides, extended-spectrum penicillins, and cephalosporins, has become a problem in many hospitals in which certain hospital-associated organisms, especially *P. aeruginosa*, colonize many patients (1, 4, 7, 8). Nosocomial infections due to aminoglycoside-resistant *P. aeruginosa* have been well documented in our own institution. Alternatives to aminoglycosides for the treatment of *P. aeruginosa* would be desirable for many clinicians whose patients harbor these resistant pathogens or are at high risk for antibiotic toxicity.

Amifloxacin (WIN 49375) is a quinolone agent chemically similar in structure to nalidixic acid, norfloxacin, and cinoxacin. The mechanism of action of these drugs is the inhibition of bacterial DNA synthesis (2). This class of compounds is more effective against gram-negative than against gram-positive organisms. They inhibit DNA synthesis in bacteria, with lesser or secondary effects on the synthesis of RNA and protein. These drugs are not known to inhibit DNA synthesis in mammalian cells.

Forty-six clinical isolates of *P. aeruginosa* were tested in this study. Of the 40 strains which were resistant to gentamicin, 7 were resistant to tobramycin, and 16 were resistant to amikacin. The organisms were recovered from urine, wound, respiratory, and blood culture specimens submitted for routine culture to the clinical microbiology laboratory at Loyola University Medical Center. No more than one isolate from any one patient was collected for this study. All isolates were stored at 4°C for up to 10 days on tryptic soy agar slants until they were tested. The antibiotics used in this evaluation were: ampicillin (Bristol Laboratories, Syracuse, N.Y.), aztreonam (E. R. Squibb & Sons, Inc., New Brunswick, N.J.), cefotaxime (Hoechst-Roussel Pharmaceuticals Inc., Somerville, N.J.), cephalexin (Eli Lilly & Co., Indianapolis, Ind.), cinoxacin (Eli Lilly), gentamicin (Schering Corp., Bloomfield, N.J.), and amifloxacin (Sterling-Winthrop, Rensselaer, N.Y.). All antibiotics were obtained in powder form, prepared in stock aqueous solutions, frozen, and maintained at −20°C until use. Susceptibility testing was performed with a standard microtiter system in which each antibiotic was diluted in Mueller-Hinton broth supplemented with calcium and magnesium (3). The concentration of each antibiotic used in the microtiter system ranged from 0.125 to 256 μg/ml, except for cephalexin and amifloxacin, which ranged from 0.0625 to 128 μg/ml. Five-hour-old broth cultures of the organisms were diluted with Mueller-Hinton broth to a standard concentration. Next, 50 μl of the standardized inoculum containing 10^5 organisms was added to wells of microtiter plates, each containing the serially diluted antibiotics in 50 μl of Mueller-Hinton broth. Two control strains were tested simultaneously with clinical isolates: *P. aeruginosa* ATCC 27853 and MGH-2. Inoculated plates were incubated at 35°C for 18 h.

Results depicting 50 and 90% MICs of all of the agents against the isolates are shown in Table 1. Amifloxacin showed excellent activity against both gentamicin-susceptible and gentamicin-resistant isolates of *P. aeruginosa* with 50 and 90% MICs of 4 and 8 μg/ml, respectively, required to inhibit the gentamicin-resistant strains (Table 1). Indeed, none of the antimicrobial agents tested were more active than amifloxacin against these resistant strains.

TABLE 1. Susceptibility results of all organisms tested

P. aeruginosa isolate	No. of isolates	50% MIC/90% MIC (μg/ml) of:						
		Amifloxacin	Gentamicin	Ampicillin	Aztreonam	Cefotaxime	Cephalexin	Cinoxacin
Gentamicin susceptible	6	2/4	1/2	>256/>256	16/32	32/32	>128/>128	>256/>256
Gentamicin resistant	40	4/8	16/64	>256/>256	32/64	128/>256	>128/>128	>256/>256

Infections with members of the family *Enterobacteriaceae* and *P. aeruginosa* which are resistant to ampicillin and cephalosporins are common in the hospital setting and frequently require aminoglycoside antibiotics (5). Furthermore, isolates of *P. aeruginosa* which are resistant to gentamicin and, in some cases, tobramycin and amikacin are being recovered more frequently as nosocomial pathogens in many hospitals. At Loyola University Medical Center, 19% of the strains of *P. aeruginosa* isolated in 1983 were resistant to amikacin, and 49% were resistant to gentamicin. New agents, such as amifloxacin, may prove very useful in the therapy of these aminoglycoside-resistant organisms.

* Corresponding author.

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